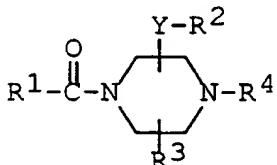


C L A I M S.

1. A compound of the formula :



wherein

Y is bond or lower alkylene,

R^1 is aryl which is substituted with 1 to 3 same or different substituent(s) selected from the group consisting of halogen, lower alkyl, lower alkoxy, mono(or di or tri)halo(lower)alkyl, nitro, amino, lower alkylamino, di(lower)alkylamino, lower alkylthio, lower alkylsulfonyl, cyclo(lower)alkylsulfonyl, aminosulfonyl, lower alkylaminosulfonyl, di(lower)alkylaminosulfonyl, pyrrolidinylsulfonyl, morpholinylsulfonyl, pyrrolylsulfonyl, pyridylsulfonyl, pyrrolyl and pyridyl;

R^2 is aryl which is substituted with 1 to 3 same or different substituent(s) selected from the group consisting of lower alkyl, mono(or di or tri)halo(lower)alkyl, mono(or di or tri)halo(lower)alkylsulfonyloxy, halogen, lower alkylenedioxy, lower alkoxy, lower alkoxy carbonyl, lower alkoxy(lower)alkoxy(lower)alkoxy, hydroxy, diphenyl(lower)alkylsilyloxy, tri(lower)alkylsilyloxy, hydroxy(lower)alkyl, cyano, amino, [mono(or di or tri)halo(lower)alkylcarbonyl]amino, lower alkylamino, N-(lower alkyl)-[mono(or di or

tri)halo(lower)alkylcarbonyl]amino, pyrrolidinyl and morpholinyl which may be substituted with lower alkoxy(lower)alkyl or lower alkyl;

5 R^3 is hydrogen or lower alkyl; and

R^4 is (3-pyridyl)methyl;

(3-pyridyl)ethyl;

3-(3-pyridyl)propyl;

3-(3-pyridyl)propenyl;

3-(3-pyridyl)propynyl;

10 thiazolyl(lower)alkyl, 1,2,4-

thiadiazolyl(lower)alkyl or 1,2,4-

oxadiazolyl(lower)alkyl, each of which is substituted with halogen, amino, lower alkylamino or di(lower)alkylamino;

15 pyrazolylmethyl which may be substituted with triphenyl(lower)alkyl or hydroxy(lower)alkyl;

pyrazolyl(lower)alkyl which is substituted with lower alkyl,

20 lower alkoxy(lower)alkylmorpholinyl(lower)alkyl or lower alkoxy(lower)alkylmorpholinylcarbonyl-(lower)alkyl;

pyrrolidinyl(lower)alkyl which is substituted with 1 or 2 same or different substituent(s) selected from the group consisting of hydroxy,

25 hydroxy(lower)alkyl, lower alkoxy and lower alkoxy(lower)alkyl;

piperidylmethyl;

30 piperidyl(lower)alkyl which is substituted with 1 or 2 same or different substituent(s) selected from the group consisting of halogen, lower alkyl and lower alkoxy(lower)alkyl;

[2,6-di[hydroxy(lower)alkyl]piperidyl](lower)alkyl;

(2,6-dimethylmorpholino)(lower)alkyl;

(2,2-dimethylmorpholino)(lower)alkyl;

35 (3,3-dimethylmorpholino)(lower)alkyl;

(cis-3,5-dimethylmorpholino) (lower)alkyl;
 ((3S,5S)-3,5-dimethylmorpholino) (lower)alkyl;
 ((3S,5R)-3,5-dimethylmorpholino) (lower)alkyl;
 (2-methoxymethylmorpholino) (lower)alkyl;
 5 (3-methoxymethylmorpholino) (lower)alkyl;
 (2-methoxymethyl-5-methylmorpholino) (lower)alkyl;
 (2-methoxymethyl-5,5-dimethylmorpholino) (lower)-
 alkyl;
 (3,5-dimethoxymethylmorpholino) (lower)alkyl;
 10 (2,2-dimethoxymethylmorpholino) (lower)alkyl;
 (2,3-dimethoxymethylmorpholino) (lower)alkyl;
 (2,6-dimethoxymethylmorpholino) (lower)alkyl;
 (2-methoxymethylmorpholino) (lower)alkenyl;
 15 (3,3-dimethylmorpholino) (lower)alkynyl;
 (2-methoxymethylmorpholino) (lower)alkynyl;
 (2-methoxymethyl-5-methylmorpholino) (lower)alkynyl;
 quinoly(lower)alkyl;
 [1H-pyrrolo[3,2-b]pyridinyl] (lower)alkyl;
 [4,5,6,7-tetrahydrothieno[3,2-c]pyridinyl] (lower)-
 20 alkyl;
 [3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl] (lower)-
 alkyl;
 (5,6,7,8-tetrahydro-1,6-naphthyridin-6-yl) (lower)-
 alkyl; or
 25 lower alkyl which is substituted with a saturated
 heterocyclic group of the formula :

30
 (wherein
 r, s and t are each integer
 of 1 to 2, and
 q is integer of 0 to 2)
 which may be substituted with one or two lower
 35 alkyl,

provided that when
R⁴ is 3-(3-pyridyl)propyl;
3-(3-pyridyl)propenyl;
5 pyrazolylmethyl which may be substituted with
hydroxy(lower)alkyl;
(2-methoxymethylmorpholino)(lower)alkyl;
(3-methoxymethylmorpholino)(lower)alkyl; or
(2-methoxymethylmorpholino)(lower)alkynyl, then
R² is not di(lower)alkylphenyl,
10 and a salt thereof.

2. The compound of claim 1, in which
Y is lower alkylene;
R¹ is phenyl which is substituted with 1 or 2 same
15 or different substituent(s) selected from the group
consisting of halogen, lower alkyl, lower alkoxy,
mono(or di or tri)halo(lower)alkyl, nitro, amino,
lower alkylamino, di(lower)alkylamino, lower
alkylthio, lower alkylsulfonyl,
20 cyclo(lower)alkylsulfonyl, aminosulfonyl, lower
alkylaminosulfonyl, di(lower)alkylaminosulfonyl,
pyrrolidinylsulfonyl, morpholinylsulfonyl,
pyrrolylsulfonyl, pyridylsulfonyl, pyrrolyl and
pyridyl;

25 R² is phenyl which is substituted with 1 or 2 same
or different substituent(s) selected from the group
consisting of lower alkyl, mono(or di or
tri)halo(lower)alkyl, mono(or di or
30 tri)halo(lower)alkylsulfonyloxy, halogen, lower
alkylenedioxy, lower alkoxy, lower alkoxycarbonyl,
lower alkoxy(lower)alkoxy(lower)alkoxy, hydroxy,
diphenyl(lower)alkylsilyloxy,
35 tri(lower)alkylsilyloxy, hydroxy(lower)alkyl,
cyano, amino, [mono(or di or
tri)halo(lower)alkylcarbonyl]amino, lower

alkylamino, N-(lower alkyl)-[mono(or di or tri)halo(lower)alkylcarbonyl]amino, pyrrolidinyl and morpholinyl which may be substituted with lower alkoxy(lower)alkyl or lower alkyl;

5 R³ is hydrogen; and

R⁴ is 3-(3-pyridyl)propyl;

3-(3-pyridyl)propynyl;

(2,6-dimethylmorpholino) (lower)alkyl;

(3,3-dimethylmorpholino) (lower)alkyl;

10 (cis-3,5-dimethylmorpholino) (lower)alkyl;

((3S,5S)-3,5-dimethylmorpholino) (lower)alkyl;

((3S,5R)-3,5-dimethylmorpholino) (lower)alkyl;

(2-methoxymethylmorpholino) (lower)alkyl;

(3-methoxymethylmorpholino) (lower)alkyl;

15 (2-methoxymethyl-5-methylmorpholino) (lower)alkyl;

(2-methoxymethyl-5,5-dimethylmorpholino) (lower)-alkyl;

(3,5-dimethoxymethylmorpholino) (lower)alkyl;

(2,3-dimethoxymethylmorpholino) (lower)alkyl; or

20 (2-methoxymethylmorpholino) (lower)alkenyl,

provided that when

R⁴ is 3-(3-pyridyl)propyl;

(2-methoxymethylmorpholino) (lower)alkyl; or

(3-methoxymethylmorpholino) (lower)alkyl, then

25 R² is not di(lower)alkylphenyl.

3. The compound of claim 2, in which

Y is C₁-C₄ alkylene;

R¹ is bis[mono(or di or tri)halo(C₁-C₄)alkyl]phenyl;

30 R² is phenyl which is substituted with 1 or 2 same

or different substituent(s) selected from the group consisting of C₁-C₄ alkyl, mono(or di or tri)halo(C₁-C₄)alkyl, halogen, C₁-C₄ alkoxy and hydroxy;

35 R³ is hydrogen; and

~~R⁴ is 3-(3-pyridyl)propyl;
3-(3-pyridyl)propynyl;
(2,6-dimethylmorpholino) (C₁-C₄) alkyl;
(2-methoxymethylmorpholino) (C₁-C₄) alkyl;
(3-methoxymethylmorpholino) (C₁-C₄) alkyl; or
(2-methoxymethyl-5-methylmorpholino) (C₁-C₄) alkyl,
provided that when
R⁴ is 3-(3-pyridyl)propyl;
(2-methoxymethylmorpholino) (C₁-C₄) alkyl; or
(3-methoxymethylmorpholino) (C₁-C₄) alkyl, then
R² is not di(C₁-C₄) alkylphenyl.~~

4. A compound of claim 3, which is selected from the group consisting of

15 (1) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[2-[(3R)-3-(methoxymethyl)morpholino]-ethyl]piperazine,
(2) 1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-(cis-2,6-dimethylmorpholino)ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,
20 (3) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[2-[(2S,9S)-2-methoxymethyl-5-methylmorpholino]ethyl]piperazine,
(4) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[3-(3-pyridyl)-2-propynyl]piperazine,
25 (5) 1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,
(6) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,
30 (7) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[3-(3-pyridyl)propyl]piperazine,
(8) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(4-chloro-3-hydroxybenzyl)-4-[2-[(2S)-2-(methoxymethyl)morpholino]-

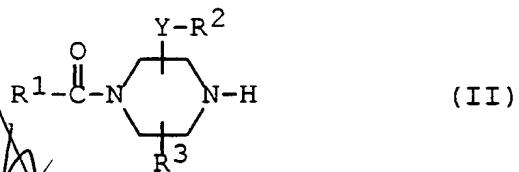
ethyl]piperazine,

(9) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(4-fluoro-3-methoxybenzyl)-4-[2-[(2S)-2-(methoxymethyl)morpholino]-ethyl]piperazine, and

5 (10) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-[4-(trifluoromethyl)benzyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]piperazine,
or a pharmaceutically acceptable salt thereof.

10 5. A process for the preparation of the compound of claim 1 or a salt thereof, which comprises,

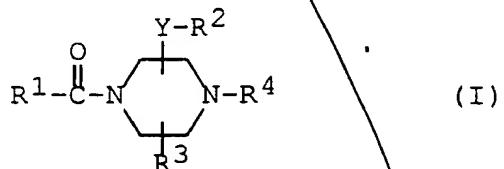
(1) reacting a compound of the formula (II) :



20 wherein R¹, R², R³ and Y are each as defined in claim 1, or a salt thereof, with a compound of the formula (III) :



25 wherein R⁴ is as defined in claim 1 and
W₁ is a leaving group,
or a salt thereof to give a compound of the formula (I) :



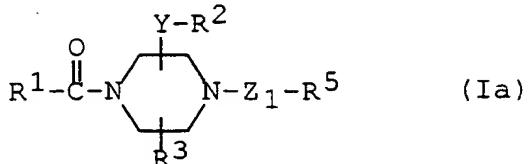
35 wherein R¹, R², R³, R⁴ and Y are each as defined in

claim 1,

or a salt thereof, or

(2) subjecting a compound of the formula (Ia) :

5



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wherein R¹, R², R³ and Y are each as defined above,

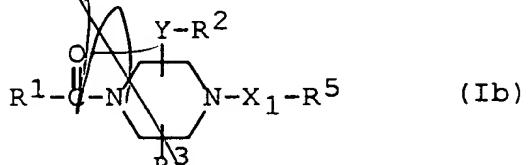
R⁵ is 3-pyridyl, and

Z₁ is lower alkynylene,

15

or a salt thereof to a reduction reaction to give a compound of the formula (Ib) :

20



25

wherein R¹, R², R³, Y and R⁵ are each as defined above,
and

X₁ is lower alkylene,

30

or a salt thereof.

30

6. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers.

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7. A compound of claim 1 for use as a medicament.

8. A method for treating or preventing Tachykinin-mediated diseases which comprises administering an effective

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~~amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof to human being or animals.~~

9. A compound of claim 1 for use as Tachykinin antagonist.

10. Use of a compound of claim 1 for manufacture of a medicament for treating or preventing Tachykinin-mediated diseases.

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